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08/470,489	06/06/95	MONTAGNIER	2356.0014-09

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PARKIN, J EXAMINER	
ART UNIT	PAPER NUMBER
1813	

DATE MAILED:
07/09/96

Please find below a communication from the EXAMINER in charge of this application.

Commissioner of Patents

Office Action Summary	Application No. 08/470,489	Applicant(s) Montagnier et al.
	Examiner Jeffrey S. Parkin, Ph.D.	Group Art Unit 1813

☒ Responsive to communication(s) filed on *3/28/96* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *42-49, 52-59, and 62-71* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *42-49, 52-59, and 62-71* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 6

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Response to Amendment under 37 C.F.R. § 1.115

1. Acknowledgement is hereby made of the amendment filed March 20, 1996, wherein claims 50, 51, 60, and 61 were canceled, claims 42, 44-49, 52, and 54-59 amended, and new claims 62-71 introduced. In the instant application claims 42-49, 52-59, and 62-71 are pending.

2. Applicants requested clarification concerning priority rights under 35 U.S.C. §§ 119 and 120. Applicants contend that the present claims receive full support in application Serial No. 06/835,228, filed March 3, 1996, and the foreign application FR 86.04215, filed March 24, 1986. All the indicated domestic and foreign priority documents have been reviewed. However, the instantly claimed invention does not receive appropriate support in any of these specifications. Applicants are directed towards application Serial No. 07/003,764, filed January 16, 1987, which discloses precise nucleotide sequences obtained from the HIV-2_{ROD} LTR, *gag*, and *env* regions. Appropriate amendment of the claim language in view of this document should be considered.

3. Claims 42-49, 52-59, and 62-71 stand rejected under 35 U.S.C. § 112, first paragraph, for the reasons of record in Paper No. 5 and as enumerated below. Applicants traversal can be summarized succinctly as follows:

(1) The claims language is enabled for a broad recitation directed towards any "probe" complementary to HIV-2 RNA because applicants

obtained similar results with HIV-2_{MIR} probes, the invention is fairly considered to be a pioneering invention based upon legal precedence and scientific data, and the use of a standard experimental was employed.

(2) The claim language has been amended to recite a washing step that involves "non-stringent" washing conditions.

(3) The claim language has been amended to identify the precise genomic location and nucleotide fragment thereby obviating this portion of the rejection.

(4) Applicants assert that one of ordinary skill in the art would be able to make all of the instantly claimed cDNA probes.

Applicants arguments have been thoroughly considered but are not deemed persuasive for the reasons of record in Paper No. 5 and as enumerated below.

The broadly recited claim language is directed towards any probe that "comprises nucleic acid complementary to HIV-2 RNA". However, the specification does not provide any guidance pertaining to the selection of probes that would function in the recited method. The claim language encompasses full-length genomic sequences, sub-genomic fragments, and oligonucleotides of varying lengths. The ability to detect HIV-2 RNA will be contingent upon the precise sequence selected and the source of the nucleic acid. According to the present claim language, any nucleic acid (i.e. cellular or viral) that hybridizes with HIV-2 RNA would be encompassed. However, the specification fails to teach the corresponding genomic locations

(i.e. LTR, *gag*, *pol*, *env*, etc.), precise nucleotide sequences, lengths, and specificity of said probes that would function in the recited assay. Are these sequences specific for HIV-2 RNA? Applicants are invited to identify those specific probes that function in the recited method and their method of construction.

The instantly claimed invention recites HIV-2 nucleic acid probes (without disclosing the actual nucleotide sequence) that comprise sequences capable of encoding for a recited amino acid sequence. As previously disclosed in Paper No. 5 "The degeneracy of the genetic code is well-recognized in the art. It has also been established that the *Lentivirinae* display considerable genomic heterogeneity. The broadly recited claim language encompasses a myriad number of combinations." However, the specification does not provide any guidance pertaining to the identification of nucleic acid sequences that encode the recited peptides.

Furthermore, the specification does not provide any guidance pertaining to the selection of appropriate hybridization and washing conditions under which the purported probes would successfully detect HIV-2 RNA. It was clearly stated in the previous office that:

> The hybridization conditions and washing conditions are critical for hybridization studies. Said conditions will vary considerably depending upon the probe size, it's genomic location (i.e. LTR vs. *env*), G-C content, and the corresponding melting temperature (T_m). In the absence of proper guidance said probes could display cross-hybridization to SIV, HIV-1, and cellular RNAs as well. Accordingly, one practicing the invention as currently claimed would incorrectly identify HIV-1 or SIV as HIV-2. This rejection may be obviated by clearly disclosing the hybridization and washing conditions (i.e. high stringency wash consisting of 0.1X SSC, 0.1% SDS at 65 degress for 30

> min. or low stringency wash consisting of 2X SSC, 0.1% SDS at 50 degress for 30 min.) of the claimed method.

Applicants have not addressed any of these critical parameters.

Finally, the invention also recites cDNA probes that may be employed in the instantly claimed method. However, the specification is silent pertaining to the generation, selection, and appropriate hybridization conditions of said cDNAs. This issue was adequately addressed in Paper No. 5 where it was noted that:

> The term "cDNA" is defined in the art as a product consisting of a double-stranded DNA sequence obtained by the *in vitro* enzymatic conversion (via reverse transcriptase) of mRNA into double-stranded DNA. However, the applicants only disclose the generation of one specific cDNA clone, pSPE2. The remaining nucleic acids (pROD 27-5, pROD 35-3, pROD 4.6, pROD 4.8, and pROD 4.7) described in the specification were generated from genomic DNA libraries and are not cDNA probes. Nucleic acid sequences corresponding to other cDNAs are not taught in the specification.

It is well known in the art that genomic viral RNAs contain considerable secondary structure that impedes the ability of reverse transcriptase to synthesize a corresponding cDNA. It seems quite improbable that the skilled artisan could generate a cDNA corresponding to the full-length viral genome, *gag*, *pol*, or *env*. Which cDNA probes should be employed in the recited assay?

The legal considerations that govern enablement determinations are disclosed in *Ex parte Forman* 230 USPQ 546-549 (PTO Bd. Pat. App. Int., 1986). The board addressed these factors and concluded the following:

> The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the

> nature of the invention and the state of the art: *Ansul Co. v. Uniroyal, Inc.*, supra. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 CCPA 1593, 347 F.2d 574, 146 USPQ 218 (1965); *In re Colianni*, supra.

When all of the aforementioned issues are considered *in toto*, it would clearly require undue experimentation the skilled artisan to ascertain all the scientific parameters required to practice the instantly claimed invention. Therefore, the rejection of claims 42-49, 52-59, and 62-71 under 35 U.S.C. § 112, first paragraph, is maintained.

4. The previous rejection of claims 42-49 and 52-59 under 35 U.S.C. § 112, second paragraph, is hereby withdrawn in response to applicants' amendment.

5. Claims 42, 52, and 62 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Clavel et al. (1986, Science 233:343-346). Applicants argued that the claimed invention receives support in the domestic priority document Serial No. 06/933,184, filed November 21, 1993. However, the instantly claimed invention is not enabled as

disclosed *supra* and does not receive the benefit of earlier filing dates. Accordingly, claims 42, 52, and 62 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Clavel et al. (1986, Science 233:343-346) as previously disclosed.

6. Claims 42-44, 52-54, and 62-64 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Clavel et al. (1986, Nature 324:691-695). Applicants argued that the claimed invention receives support in the domestic priority document Serial No. 06/933,184, filed November 21, 1993. However, the instantly claimed invention is not enabled as disclosed *supra* and does not receive the benefit of earlier filing dates. Accordingly, claims 42-44, 52-54, and 62-64 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Clavel et al. (1986, Nature 324:691-695) as previously disclosed.

7. The *provisional* rejection of claims 42-49, 52-59, and 62-71 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 42-46 and 48-50 of copending application Serial No. 08/392,613 is hereby maintained for the reasons of record in Paper No. 5. Applicants are invited to provide a copy of the restriction requirement made in application Serial No. 07/792,524, filed November 18, 1991, demonstrating that these claims are patentably distinct. Absent evidence to the contrary, this rejection is hereby maintained.

8. Claims 42, 49, 52, 59, 62, and 69 stand *provisionally* rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 83 of copending application Serial No. 08/250,103 for the reasons of record in Paper No. 5.

New Grounds of Rejection

9. Originally presented claims 42-49 and newly submitted claims 62-69 are rejected under 35 U.S.C. § 112, second paragraph, as being multiplicative (refer to M.P.E.P. § 2173.05(n)). Claims 42-49 and 62-69 are merely duplicates of each other. Both sets of claims are directed towards methods of detecting HIV-2 retroviral RNA employing nucleic acid probes that are complementary to HIV-2 RNA. The claims are clearly of the same breadth and scope.

10. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

11. Correspondence related to this application may be submitted to Group 1813 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax number for Group 1813 is **(703) 305-7939**. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

12. Any inquiry concerning this communication should be directed to **Jeffrey S. Parkin, Ph.D.** whose telephone number is **(703) 308-2227**. The examiner can normally be reached Monday through Friday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, **Ms. Christine Nucker** can be reached at **(703) 308-4028**. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1813 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Group Art Unit 1813

June 23, 1996

ROBERT D. BUDENS
PRIMARY EXAMINER
GROUP 1800